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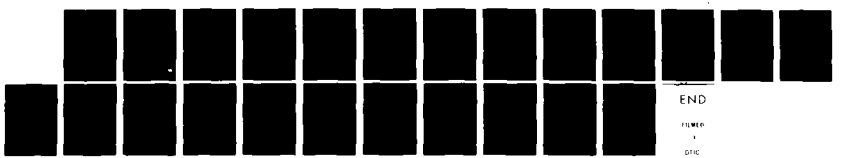

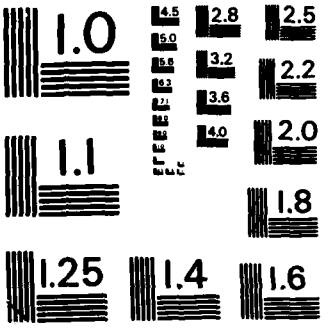

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THE USAFSAM CARDIOVASCULAR DISEASE FOLLOWUP STUDY: CLINICAL EVALUATION OF SUBJECTS NEAR AGE 43

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August 1982

Interim Report for Period December 1975 - January 1980

USAF SCHOOL OF AEROSPACE MEDICINE
Aerospace Medical Division (AFSC)
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NOTICES

This interim report was submitted by personnel of the Clinical Pathology Branch, Clinical Sciences Division, USAF School of Aerospace Medicine, Aerospace Medical Division, AFSC, Brooks Air Force Base, Texas, under job order 7755-17-48.

When U.S. Government drawings, specifications, or other data are used for any purpose other than a definitely related Government procurement operation, the Government thereby incurs no responsibility nor any obligation whatsoever; and the fact that the Government may have formulated, furnished, or in any way supplied the said drawings, specifications, or other data is not to be regarded by implication or otherwise, as in any manner licensing the holder or any other person or corporation, or conveying any rights or permission to manufacture, use, or sell any patented invention that may in any way be related thereto.

The voluntary informed consent of the subjects used in this research was obtained in accordance with AFR 169-3.

This report has been reviewed by the Office of Public Affairs (PA) and is releasable to the National Technical Information Service (NTIS). At NTIS, it will be available to the general public, including foreign nations.

This technical report has been reviewed and is approved for publication.

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20. ABSTRACT (Continue on reverse side if necessary and identify by block number)

Clinical examinations were performed on 382 members of the Cardiovascular Disease Followup Study (West Point Study). Four men (of eight who underwent cardiac catheterization during the examination) were found by coronary angiography to have significant coronary disease. Previously another man had undergone coronary bypass surgery after an evaluation by coronary angiography and five men had suffered a myocardial infarction (documented by medical records and electrocardiographic evidence). Unequivocal evidence of coronary artery disease was therefore present in ten men.

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20. ABSTRACT (Continued)

The pattern of means of serum lipid and lipoprotein levels expected to be associated with coronary artery disease was found in this disease group; however, because of the biological variability and the small number of men in the disease group, no definite conclusions were drawn about the meaning of these risk factors in this group. A summary of extensive laboratory data collected on the other members of the group is essentially a table of normal values for healthy men at approximately 43 years of age.

The members of this study are not a cross section of U.S. males of comparable age. This fact may be responsible for the disproportionately high prevalence of type A1 behavior pattern and the finding that the type A behavior pattern was not highly correlated with elevation of any of the common risk factors for coronary artery disease. More followup studies will be required to capitalize on the potentially important contribution this study can make to understanding the relationship between an individual's history of changes in risk factor levels and the development of cardiovascular disease.

THE USAFSAM CARDIOVASCULAR DISEASE FOLLOWUP STUDY: CLINICAL EVALUATION OF SUBJECTS NEAR AGE 43

BACKGROUND

The USAF School of Aerospace Medicine (USAFSAM) initiated the Cardiovascular Disease Followup Study in 1952 "to obtain information on the relationship of various lipid components of the blood to the occurrence of atherosclerotic heart disease" (1). This information would not only be of national importance, it would also be extremely important in selecting candidates for pilot training if serum lipid/lipoprotein levels could be used to identify candidates whose useful time as pilots would be cut short by atherosclerotic heart disease. Pilot training is very costly, and significant savings could be effected by not training individuals with a high risk of being grounded within a few years by symptoms of cardiovascular disease.

The plan adopted was to measure serum cholesterol, phospholipid, and lipoprotein levels in a group of 18-20-year-old men and to repeat these measurements in these same men every 2 years throughout their lifetime (2). The subjects in the study entered the United States Military Academy (USMA) at West Point in 1952 and were graduated in 1956. Since graduation, they have had biennial physical examinations: medical findings and health histories, smoking habits, physical activity levels, stress levels, etc., were recorded. Also, their blood has been analyzed biennially for lipid and lipoprotein levels (3,4).

A significant feature of the original plan was to use tissues obtained at autopsy to evaluate the extent of atherosclerotic heart disease in each subject. This information would be correlated with the lipid and lipoprotein levels and other pertinent medical information obtained during the life of each individual. The correlation would permit an assessment of how well the extent of the atherosclerotic process had been reflected in the serum lipid/lipoprotein levels and in the development of recognized symptoms of cardiovascular disease in that individual.

In this plan, hard evidence for atherosclerotic heart disease in any subject would be the appearance of recognized symptoms (preferably documented by changes in the electrocardiogram) and the findings in the tissues collected at autopsy. In asymptomatic subjects, the meaning of the history of lipid/lipoprotein levels would be assessed almost entirely by the results of the tissue examinations. Since the subjects are a military population, they frequently travel widely on duty or for personal business or pleasure. A significant number will probably die in circumstances such that tissues will not be recovered at autopsy. To depend entirely on autopsies, therefore, is to risk losing much of the study's value because of loss of endpoint data.

This consideration, coupled with the great progress made between 1952 and 1974 in the techniques of evaluating cardiovascular disease in living individuals, prompted an invitation to the subjects to visit the USAFSAM for a thorough cardiovascular examination. The purpose of this examination was to obtain an objective evaluation of the status of the cardiovascular system of each subject, using the tools and skills of modern cardiology supported by appropriate related medical specialties. This paper reports the general findings of these examinations.

MATERIALS AND METHODS

The subjects were males, ages 41-48 (mean = 43.4) years, who had been graduated from the USMA in 1956. Of the 474 members of the study in 1956, 27 were dead by 1974 and 47 no longer participated in the study. Of the 400 remaining participants, 382 came to the USAFSAM for the voluntary cardiovascular examination during the years 1975-1978. Three who declined the examination are known to have been concerned about the potential for discovery of a health problem that would jeopardize their military position(s). The prevalence of heart disease in the individuals who declined cannot be determined. During the week preceding their examination, subjects were instructed to follow their normal patterns of eating and exercise. All were further instructed to eat a regular dinner early in the evening preceding the examination and not to eat again until after the fasting blood sample was drawn at 0745 the following morning. Each subject was requested to keep a 3-day diet diary covering a Sunday-Tuesday period at least 1 week before the examination was scheduled. As part of the examination protocol, this record was reviewed with the subject by a dietitian.

Each subject recorded his family and personal medical history during an interactive session with a computer program. This information was obtained to verify previously reported medical data. The results of this computerized questionnaire were reviewed with each subject by his examining physician.

Each subject was examined by one of seven physicians who conducted all the physical examinations of the subjects during the 3-year span of the effort. The physician took the history, performed the physical examination, and referred the subject to various subspecialties as required to evaluate any of the medical findings.

An interview was conducted to determine whether the subject exhibited type A1, A2, X, or B behavior pattern, according to the Rosenman-Friedman classification (5) of coronary-prone behavior patterns. This interview was conducted by a nurse who had been trained by Dr. Ray Rosenman, and was recorded on videotape. The nurse rated the behavior pattern. Dr. Rosenman, as the consulting expert, viewed the playback of the interview and, knowing the nurse's rating but none of the subject's medical data, also rated the behavior pattern.

The entire protocol is outlined in Table 1. The laboratory analyses and the method for each analysis are listed in Table 2.

TABLE 1. PROTOCOL FOR CLINICAL EVALUATION

I. History

- A. Routine (with cardiovascular emphasis)
- B. Dietary (form plus interview with dietitian)
- C. Risk Factors (branching logic computer program)
  Family and personal history, habits, negative life factors, and risk taking

II. Physical Examination

- A. Routine Aeromedical Examination
- B. Ophthalmology
- C. Subspecialties (only as indicated by findings)

III. Testing

- A. X-ray (PA and L. lateral chest, and KUB)
- B. Body Composition (by ^{40}K count and anthropometric measurements)
- C. Laboratory
  1. CBC
  2. Tissue destruction screen
     a. ESR
     b. Serum protein (electrophoresis if indicated)
     c. LDH isoenzymes (only if indicated)
  3. Hepatic screen
     a. Bilirubin - total and direct
     b. Enzymes - SGOT, SGPT, GGTP, alkaline phosphatase
     c. ICG (only if indicated)
  4. Lipids
     a. Automated methods
        Cholesterol, triglycerides, phospholipids, total lipids
     b. Old methods
        Cholesterol
        Lipoproteins by ultracentrifuge
  5. Renal screen
     a. Urinalysis
     b. BUN
     c. Creatinine
  6. Metabolic
     a. Uric acid
     b. Thyroid (T3 and T4)
     c. Glucose tolerance fasting; 30-, 60-, 90-, and 120-min samples
        Measure glucose and cortisol levels
     d. K^+, Na^+, Ca^+, and Mg^+

IV. Procedures

- A. Cardiovascular
  1. Resting ECG and Holter monitor
  2. Resting VCG
  3. Double Masters exercise test
  4. Treadmill exercise test
  5. Phono-, angio-, and echocardiogram (as indicated)
  6. Cardiac catheterization (seldom, only if justified by finding)
- B. Pulmonary Function
  1. VC, FEV, FEV_3, MVV
  2. If abnormal: bronchodilators, volumes, DL_{CO}, N_2 washout
- C. Behavior Pattern (interview recorded on videotape)

TABLE 2. LABORATORY METHODS

Test	Method/Instrument Used*
Complete Blood Count (CBC)	Coulter counter Model Fn or J. T. Baker hematology analyzer Model 500 (6)
Hemoglobin**	Coulter hemoglobinometer (6)
Hematocrit**	Wintrobe (7)
Blood cell morphology	Wintrobe (8)
Reticulocyte count	Wintrobe (8)
Sedimentation rate	Wintrobe (9)
Serum	
Haptoglobins	Owen et al. (10), adapted to Technicon AutoAnalyzer II
Total proteins	Refractometer (11)
Albumin and globulins	Beckman electrophoresis, cellulose acetate (12)
Enzymes	
SGOT	Amador-Wacker (13), Worthington Diagnostics
SGPT	Henry et al. (14), Worthington Diagnostics
GGTP	Szasz (15), Worthington Diagnostics
LDH	Wacker-Amador (16), Worthington Diagnostics
Alkaline phosphatase	Bowers-McComb (17), Worthington Diagnostics
LDH isoenzymes	Beckman electrophoresis, cellulose acetate (18)
Bilirubin, direct and total	Jendrassik-Grof (19), AutoAnalyzer II
Blood Urea Nitrogen (BUN)	Marsh-Miller (20), AutoAnalyzer II
Creatinine	Stevens-Skeggs (21), AutoAnalyzer II
Uric Acid	Technicon AutoAnalyzer, Laboratory File NI3b (22)
Inorganic Phosphorus	Technicon AutoAnalyzer II, Clinical Method 04 (23)
K^+, Na^+, CO_2, Cl^-	Technicon Instruments Stat-Ion (24)
Ca^{++}, Mg^{++}	Perkin-Elmer atomic absorption Model 303 (25)
Lipids	
Cholesterol	Lieberman-Burchard, adapted (26)
Triglyceride and cholesterol	Automated for AutoAnalyzer by Wease et al. (27)
Phospholipid P	Total P *minus* inorganic P (28)
Total lipids	Calculated from measured serum lipid (28)
Lipoproteins	DeLalla and Gofman (29), using ultracentrifuge
Plasma	
Glucose	Hoffman (30), AutoAnalyzer II
Cortisol	Competitive protein binding (Cortipak, Amersham-Searle)
Serum T3	T3 radioimmunoassay (31), adapted by Kay (USAFSAM/NGIR)
Serum T4	T4 radioimmunoassay (32), adapted by Kay (USAFSAM/NGIR)
Urine	
Specific gravity	Urinometer (33)
pH	Ames LabStix (34)
Protein	Ames LabStix; if elevated, use sulfosalicylic acid (35)
Glucose	Ames LabStix (34)
Acetone	Ames LabStix (34)
Blood	Ames LabStix (34)
Bile	Ames LabStix (34)
Cells, casts, etc.	Microscope (36)

* Naming of specific product or manufacturer does not constitute an endorsement of the item or company by the U.S. Air Force nor does such naming imply superiority of the item over other items of similar cost supplied by other companies.

** When the Baker hematology analyzer was used, hemoglobin and hematocrit values were included in the output from the instrument.

RESULTS AND DISCUSSION

Table 3 summarizes the laboratory findings in the men who did not present evidence of cardiovascular disease. The 2.5 and 97.5 percentiles listed were determined nonparametrically. All the mean values lie within the normal range for the USAFSAM laboratory. Table 3, therefore, is essentially a table of normal values for a group of 43-year-old military officers, most of whom were on active duty.

TABLE 3. LABORATORY VALUES FOR THE NONDISEASE GROUP

Variable	N	Mean	S.D.	Percentile 2.5	Percentile 97.5
Hematocrit	356	46.5%	2.88	41	52
Hemoglobin	371	15.4 g/dl	1.05	13.3	17.5
RBC	360	5.27x106/mm^3	0.356	4.53	5.96
MCV	357	88.7 µm	3.73	82.1	97.6
MCH	359	29.2 ng/cell	1.39	26.8	32.4
MCHC	369	33.0%	0.91	31.5	34.8
WBC	371	6329/mm^3	1904.5	3900	11200
Neutrophils	371	56.9%	8.84	41	73
Bands	371	0.7%	0.96	0	3
Lymphocytes	366	35.2%	8.63	20	52
Monocytes	366	4.6%	2.68	0	10
Eosinophils	367	2.5%	2.07	0	7
Basophils	366	0.1%	0.34	0	1
Sed Rate	371	7.3 mm/hr	5.80	1	21
Serum					
Haptoglobins	364	81.3	33.37	29	161
Total protein	370	7.3 g/dl	0.45	6.5	8.3
Albumin	370	4.3 g/dl	0.37	3.6	5.1
α-1 globulin	370	0.28 g/dl	0.061	0.2	0.4
α-2 globulin	370	0.64 g/dl	0.109	0.5	0.9
β-globulin	370	0.92 g/dl	0.155	0.6	1.2
γ-globulin	369	1.2 g/dl	0.235	0.8	1.7
Uric Acid	372	6.3 mg/dl	1.07	4.4	8.8
Creatinine	372	1.2 mg/dl	0.11	1.0	1.4
Urea Nitrogen	372	15.0 mg/dl	3.07	9.8	22.1
Bilirubin, total	371	0.9 mg/dl	0.38	0.4	1.8
Bilirubin, direct	340	0.2 mg/dl	0.11	0.09	0.54
Enzymes					
Alk phosphatase	369	47.1 mU/ml	13.24	27	69
GGTP	326	15.6 IU	12.73	5	48
SGOT	370	21.9 IU	7.52	12	43
SGPT	369	24.5 IU	11.80	10	57
LDH	358	206.6 IU	70.75	124	366
Fraction I	318	25.9%	3.67	19.2	33.4
Fraction IV	320	8.0%	2.63	3.6	14.2
Cholesterol	372	208.6 mg/dl	34.51	148	283
Triglyceride	371	124.6 mg/dl	61.81	51	284
Phospholipid	371	223.7 mg/dl	44.52	153	300
Total Lipid	370	664.5 mg/dl	158.29	470	963
Electrolytes					
Sodium	367	140.4 mEq/l	1.82	137	144
Potassium	367	4.3 mEq/l	0.30	3.7	4.9
Calcium	370	9.7 mg/dl	0.32	9.1	10.3
Magnesium	368	2.08 mg/dl	0.14	1.8	2.3
Inorganic P	372	3.35 mg/dl	0.38	2.6	4.1
Plasma					
Glucose, fasting	371	102.2 mg/dl	7.13	90	116
Glucose, 1 hr	370	136.9 mg/dl	33.99	85	216
Glucose, 1.5 hr	367	112.6 mg/dl	28.07	76	181
Glucose, 2 hr	371	99.7 mg/dl	22.56	60	150

TABLE 3 (Continued).

Variable	N	Mean	S.D.	Percentile 2.5	Percentile 97.5
Urine					
Sp. gr.	369	1.108	0.0077	1.004	1.030
pH	372	5.8	0.49	5.0	7.0
Casts, hyaline/10 LPF	371	0.87	1.719	0	6
Casts, granular/10 LPF	371	0.26	0.993	0	2
WBC/10 HPF	371	5.1	3.97*	0	18
RBC/10 HPF	371	6.2	6.11**	0	15
Plasma Cortisol					
Fasting	201	12.9 µg/dl	3.67	8	21
0.5 hr	198	10.8 µg/dl	3.83	5	20
1.0 hr	200	10.0 µg/dl	3.37	5	18
1.5 hr	201	10.4 µg/dl	3.46	5	18

* 6 subjects had values ranging between 25 and 250.

** 8 subjects had values ranging between 29 and 999.

From the point of view of need for medical care, the most significant clinical findings included the discovery of a liomyosarcoma in one subject, significant hypothyroidism in two, Type IV hyperlipoproteinemia in one, and significant obstruction of blood flow in coronary arteries in one who was previously unaware of the problem. For four men, coronary arteriography removed the implication of possible coronary artery disease raised by false positive treadmill exercise stress tests. The various other findings during the examinations are summarized in Table 4. The diagnoses listed in that table are not mutually exclusive.

Figure 1 is a histogram showing the distribution of the percent body fat in the group, as determined by the ^{40}K method (37). The men without evidence of cardiovascular disease had a mean value of 22.4% body fat. The percent body fat was not statistically correlated with the average caloric intake estimated from the 3-day diet diaries. Intakes ranged from 1159 to 4013 cal/day and averaged 2335 cal/day. The absence of a convincing relationship between percent body fat and the caloric intake per unit of lean body mass is evident in Figure 2.

Mean values for various factors related to cardiovascular disease were computed for all those with body fat > 24% and then compared with the means computed for the remainder of the subjects. Small but significant elevations in means occurred for all lipid and lipoprotein fractions ($P<.05$) except for cholesterol, which showed no difference, and for HDL, which had a slightly decreased mean ($P<.01$). Means were slightly higher for blood pressure ($P<.02$) and T3 ($P<.01$) but were not significantly elevated for fasting glucose, cortisol, and T4. Table 5 lists significant findings when correlations of percent body fat with other variables were computed for the entire 382 subjects.

TABLE 4. SUMMARY OF DIAGNOSES

Liomyosarcoma	1
Moderate Obstructive Pulmonary Disease	8
Reynaud's Phenomenon	5
ECG Diagnosis	
Supraventricular tachycardia	4
First degree A-V block	7
Second degree A-V block, A-V nodal, type I	3
Right bundle branch block	2
Terminal IV conduction defect	10
Left bundle branch block	3
Left anterior fascicular block, persistent	2
Unclassified IV conduction defect	32
Low-amplitude T waves	27
Nonspecific ST depression	17
ST-segment straightening	14
History of serial ST, T-wave changes	3
Left ventricular hypertrophy (ECG only)	8
Septal hypertrophy	3
Myocardial damage	6
Atherosclerotic Coronary Disease	10
Thyroid	
Enlargement	3
Hypothyroidism	3
Abnormal thyroid function	1
Low TSH	1
Carbohydrate	
Decreased glucose tolerance	20
Diabetes mellitus	1
Gout	4

TABLE 5. CORRELATIONS OF PERCENT BODY FAT WITH OTHER VARIABLES

Variable	Corr. Coeff.	P Value
Weight	.77	.0001
Ponderal Index	-.70	.0001
Systolic BP	.23	.0001
Diastolic BP	.26	.0001
VLDL	.35	.0001
IDL	.23	.0001
LDL	.20	.001
HDL	-.29	.0001
Chol/HDL-C	.34	.0001
Cholesterol	.15	.02
Triglyceride	.37	.0001
Phospholipid	.17	.007
Uric Acid	.30	.0001
T3	.17	.02

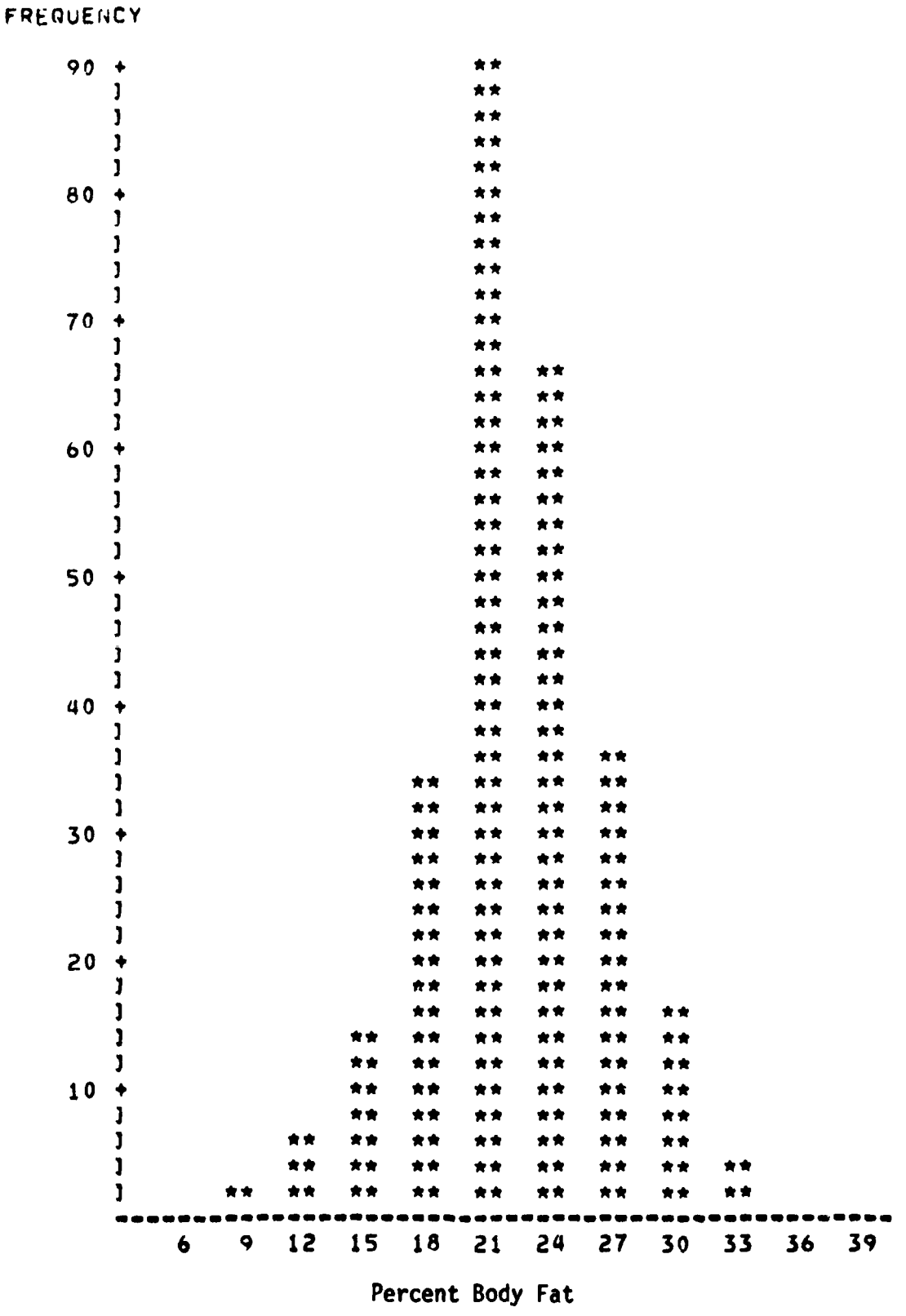

Figure 1. Histogram showing the distribution of % body fat (estimated by the ^{40}K method using the USAFSAM whole-body counter) among the 275 subjects whose body composition was measured.

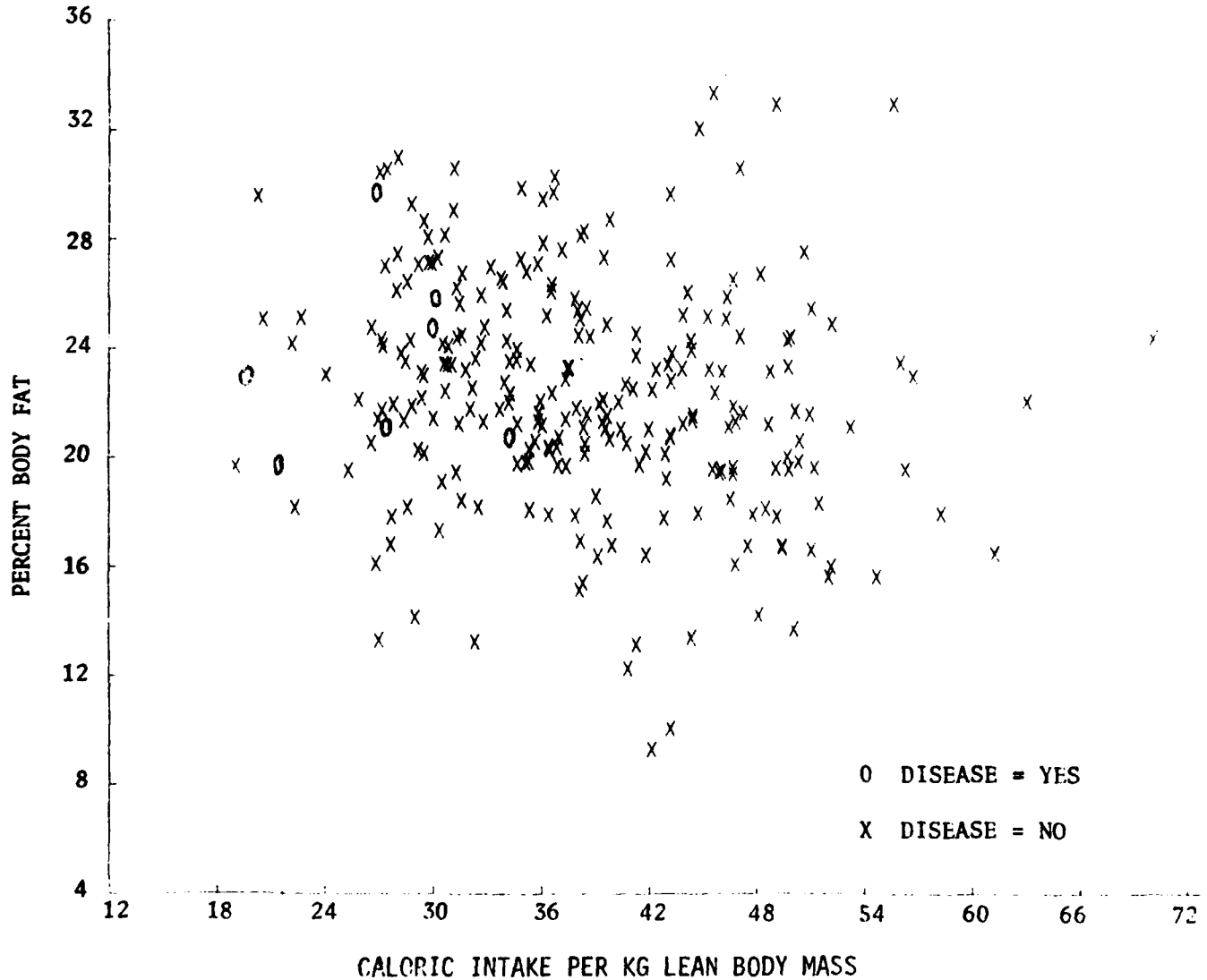

Figure 2. Plot of % body fat against caloric intake per kg of lean body mass for each of the 275 subjects for whom these data were available.

Among the 382 subjects examined, five presented a history of a previous myocardial infarction documented by medical records and electrocardiographic evidence. Five other men were found (four at USAFSAM and one elsewhere) to have coronary artery disease by the procedures summarized in Table 6.

Because of its high correlation with coronary artery disease, the ratio of total cholesterol to HDL-cholesterol (HDL-C) was computed (38). Although the HDL-C was not measured, the HDL levels were measured in the ultracentrifuge. The assumption was made that the average composition of the HDL was 20% cholesterol by weight (39), and the ratio was computed by dividing the total cholesterol level by the factor HDL X 0.2. The values for the ratios in Tables 5, 7, and 9 were computed by this procedure. Other variables recognized as risk factors for cardiovascular disease, plus variables that might impact on that risk, were tabulated for the 10 subjects found to have cardiovascular disease and for the other subjects in the study. Mean values for all variables in the two groups of subjects are listed in Table 7.

The data in Table 7 show that the disease and nondisease groups do not differ significantly ($P>.05$) in age, body habitus (height, weight, % fat, ponderal index), or serum levels of thyroid hormones, uric acid, cortisol, or fasting glucose. Levels of serum lipids and lipoproteins show the expected pattern, including higher levels of cholesterol ($P<.041$) and the less dense lipoproteins ($P<.006$), a lower mean for HDL (NS), and a higher mean for the chol/HDL-C ratio ($P<.035$) in the disease group. While this pattern is expected to be associated with coronary artery disease (40), the biological variability combined with the small number of subjects in the disease group makes it inadvisable to draw definite conclusions about the meaning of the levels of these risk factors in this disease group.

TABLE 6. IDENTIFICATION OF SUBJECTS WITH CORONARY ARTERY DISEASE (CAD) BY TREADMILL EXERCISE TOLERANCE TEST, DOUBLE MASTERS EXERCISE TEST, AND CORONARY ANGIOGRAPHY

TM[a]	DM:[a] Abnormal	Borderline	Normal	Totals
Abnormal	1/0[b]	2/1/0[b]	9/6/3[b]	12/7/3[b]
Borderline	0/0	0/0	19/1/1[c]	19/1/1[c]
Normal	1/0	6/0	339/1/1[d]	346/1/1[d]
Totals	2/0	8/1/0	367/8/5	377/9/5

[a]TM = treadmill exercise test; DM = double Masters exercise test

[b]Numbers sequences indicate number of subjects with indicated exercise response/number of these who underwent coronary angiography/number found by angiography to have CAD. Example: 9/6/3 denotes that 9 subjects had abnormal treadmill but normal double Masters tests; 6 of these underwent coronary angiography, which showed that 3 had CAD.

[c]Prior coronary bypass surgery (performed elsewhere)

[d]Prior myocardial infarction

TABLE 7. MEAN VALUES IN THE DISEASE AND NONDISEASE GROUPS*

Variable	Group	N	Mean	S.D.	Percentile 2.5	Percentile 97.5
Age (yr)	A	10	43.1	1.20		
	B	372	43.4	1.37	41	46
Smoking Years	A	5	23.2	4.71		
	B	210	16.9	7.26	3.0	30.0
Packyears	A	5	31.90	13.72		
	B	209	22.30	14.53	1.2	52.5
Height (in)	A	10	70.8	2.15		
	B	372	70.6	2.12	66.0	74.0
Weight (lb)	A	10	179.1	27.75		
	B	372	179.8	21.12	144	222
% Fat	A	8	23.0	3.63		
	B	267	22.4	4.18	13.4	30.6
Ponderal Index	A	10	12.60	0.349		
	B	372	12.54	0.429	11.62	13.32
Systolic BP	A	10	127.4	7.72		
	B	372	121.9	12.41	100	148
Diastolic BP	A	10	85.0	9.20		
	B	372	78.8	9.50	60	100
T3 (ng/ml)	A	6	117.7	47.20		
	B	256	114.9	26.38	75	180
T4 (µg/ml)	A	6	7.78	3.535		
	B	239	7.91	1.613	5.4	12.1
Uric Acid (mg/dl)	A	10	6.5	1.3		
	B	372	6.3	1.07	4.4	8.8
Cortisol (µg/dl)	A	5	12.00	1.000		
	B	201	12.88	3.670	8.0	21.0
Glucose, fast. (mg/dl)	A	10	101.0	12.88		
	B	371	102.2	7.13	90	116
Triglyceride (mg/dl)	A	10	150.5	53.15		
	B	371	124.6	61.81	51	284
Phospholipid (mg/dl)	A	10	228.7	42.33		
	B	371	222.7	44.52	153	300
Cholesterol (mg/dl)	A	10	232.7	26.26		
	B	372	209.3	34.51	148	283
VLDL (mg/dl)	A	10	124.3	72.0		
	B	371	106.1	76.65	12	315
IDL (mg/dl)	A	10	40.5	16.30		
	B	370	34.8	18.77	7	74
LDL (mg/dl)	A	10	418.6	63.01		
	B	371	343.1	84.91	194	517
HDL (mg/dl)	A	10	231.1	85.65		
	B	370	243.1	63.76	146	393
Chol/HDL-C	A	10	5.5	1.55		
	B	370	4.6	1.35	2.4	7.7

*Group A--10 men with cardiovascular disease; Group B--remaining subjects.

Mean values of variables affecting cardiovascular disease were also calculated for groups of subjects who shared certain abnormal findings. The 20 individuals with decreased glucose tolerance had slightly increased mean values for blood pressures and for serum levels of cholesterol, LDL, triglycerides, VLDL, T3, and fasting glucose. However, neither the mean level of HDL nor the mean ratio of chol/HDL-C was statistically increased ($P>.05$) over mean values for the other subjects.

Mean values in small groups of subjects with selected findings were compared with means for the remainder of the subjects. In the groups with findings on the resting electrocardiogram (ECG) of low-amplitude T waves (N=27), nonspecific ST-segment depression (N=17), or ST-segment straightening (N=14), there were small differences in the means--including depression of HDL levels and increases in levels of triglycerides, VLDL, IDL, LDL, and cholesterol, with associated increases in the ratio of cholesterol/HDL-cholesterol. Because of the variability in values, the small number of subjects, and the small differences from the means for the remaining subjects, no association of these changes with increased risk could be established.

In the early years of the Framingham study (41), electrocardiographic evidence of left ventricular hypertrophy (LVH) in middle-aged people was identified as one of the primary risk factors for heart disease. Since only eight of our subjects had ECG evidence of left ventricular hypertrophy, our data do not warrant comment about LVH as a risk factor in this group.

The relationship between behavior pattern and risk of cardiovascular disease (42) prompted the classification of the participants of this study as Type A1, A2, X, or B. As stated previously, the subjects were rated by two experts. The agreement of the two raters in the assignment of behavior pattern can be assessed from Table 8. There was exact agreement on 174 (57%) of the 303 subjects rated and serious disagreement (ratings separated by 2 or 3 classes) on only 14 (5%) of the subjects. Rater 1 classified more subjects as X, but fewer as B, than rater 2 did. The extent of concurrence in rating is particularly impressive in this group of men, all of whom had successfully completed 4 years of military training that would have placed high value on behavior patterns typical of type A. In this group, therefore, even true type B individuals might display behavior patterns normally associated with type A.

The data in Table 8 show that rater 1 classified 161 (53%) of the subjects as type A (23% A1 + 30% A2) and 43 (14%) as type B. Rater 2 classified 180 (59%) as type A (25% A1 + 34% A2) and 63 (21%) as type B. This relatively high proportion of type A1 behavior patterns (43) is consistent with the military training and the generally high military rank of the subjects in the study.

TABLE 8. COMPARISON OF BEHAVIOR PATTERN RATINGS BY TWO RATERS*

Rater 1		Rater 2:	A1	A2	X	B	Total
		N:	75	105	60	63	303
	N						
A1:	70 =		(52)	15	2	1	
A2:	91 =		22	(51)	12	6	
X:	99 =		1	35	(39)	24	
B:	43 =		0	4	7	(32)	
Total:	303						(174)

*Rater 1 = Thomas; Rater 2 = Rosenman: ( ) = agreement

Table 9 lists the mean values for various factors that impact on risk of cardiovascular disease. For rater 1, the only significant differences between the means of any of the groups were for factors HDL and LDL. Although the mean HDL was higher for group A2 than for group X, neither mean for these groups differed significantly from the means for groups A1 and B. The mean LDL was higher for group A1 than for group B, but neither mean differed significantly from the means for groups A2 and X.

For rater 2, significant differences were found between means for height, cholesterol, LDL, IDL, and T4. Group B was taller than groups A1 and X, but not than group A2. For cholesterol and IDL, the mean was significantly higher for group A1 than for group X, but not than for groups A2 and B. For LDL, the mean for group A1 was higher than for groups X and B. For T4, the mean was lower for group A1 than for group X, but neither mean differed significantly from the mean for groups A2 or B.

In general, the means for cholesterol, LDL, IDL, and VLDL were numerically higher for group A1 than for the other three groups. With larger N values, these elevations might be statistically significant. The mean cholesterol level in global group A (A1+A2) was not significantly higher than the mean for group B, but was higher ($.05>P>.01$) than the mean for group X and the mean for combined group (X+B). The overall lack, or low level, of statistical significance between most groups emphasizes the fact that the differences between the mean values were not large compared to the range of values within the groups. Consequently, in this particular group of men, behavior pattern is not highly correlated with recognized factors of risk for cardiovascular disease. This finding is underscored by the lack of significant differences among the behavior pattern groups in levels of such risk correlates as serum cortisol, uric acid, HDL, and cholesterol/HDL-C ratios.

Of the 10 subjects with coronary artery disease, 8 were interviewed for behavior pattern. The ratings for these men are 50% type A1 + A2 by rater 1 and 38% type A1 (no type A2) by rater 2. Of the 294 subjects without coronary artery disease who were interviewed, 23% were rated as type A1 and 30% as type A2 by rater 1. The corresponding values for rater 2 were 24% type A1 and 35% type A2.

TABLE 9. RISK FACTOR MEANS IN BEHAVIOR PATTERN GROUPS

Variables	Behavior Group:	Rater 1 A1	Rater 1 A2	Rater 1 X	Rater 1 B	Rater 2 A1	Rater 2 A2	Rater 2 X	Rater 2 B
N		70	91	99	43	75	105	60	63
Age (yr)		43.5	43.1	43.4	43.6	43.4	43.4	43.2	43.4
Height (in)		70.3	70.3	71.0	70.8	70.2	70.6	70.4	71.2
Weight (lb)		181.1	178.8	179.0	180.9	179.3	181.9	174.5	181.7
Ponderal Index		12.5	12.5	12.6	12.6	12.5	12.5	12.6	12.6
% Fat		22.6	21.7	23.1	22.8	21.9	22.7	22.4	23.4
Systolic BP		124.4	122.2	121.3	120.8	123.4	123.6	120.1	120.4
Diastolic BP		81.0	78.7	78.4	78.3	80.4	79.0	77.9	78.6
T3		119.9	116.7	117.6	110.1	119.7	113.5	123.4	112.9
T4		7.5	8.1	7.9	8.1	7.5	8.0	8.3	7.9
Uric Acid		6.4	6.4	6.2	6.1	6.3	6.4	6.3	6.1
Cortisol		10.3	11.1	11.6	10.0	10.5	11.0	11.1	11.1
Fasting Glucose		102.8	101.4	101.8	102.9	101.9	102.2	101.5	102.6
Triglycerides		136.2	125.2	122.8	121.3	138.4	122.5	115.9	128.6
Phospholipids		227.5	222.9	224.1	219.2	130.4	111.3	217.5	222.3
Cholesterol		215.4	209.0	209.2	203.3	216.7	211.7	202.6	204.9
Lipoproteins									
VLDL		120.3	104.0	108.8	102.9	119.1	105.8	97.4	114.3
IDL		37.9	34.6	33.6	33.3	38.0	34.4	30.2	36.3
LDL		367.0	342.6	347.2	323.8	366.6	349.7	332.1	333.7
HDL		240.3	253.7	229.8	235.4	246.1	238.5	238.3	236.7
Chol/HDL-C		4.5	4.5	5.0	4.5	4.5	5.0	4.5	4.5

For the group of means for each variable, underlining is used only if one or more means differ statistically. In such instances, means that are statistically similar (do not differ statistically) are underlined with the same type of line (dotted or solid). Only for height were the differences among means significant at the P=.01 level; all other differences were significant at only the P=.05 level.

To assess whether cigarette smoking was associated with risk of heart disease in the entire group, subjects were classified as smokers (currently smoke cigarettes) or nonsmokers (have not smoked cigarettes for at least 1 year). Mean values of the variables are presented in Table 10. These means do not differ significantly for the two groups for physical characteristics (height, weight, ponderal index) or for blood pressures ($P<.05$). Although the mean HDL level was lower for smokers than for nonsmokers, the difference was not statistically significant by itself ($P<.05$). However, the total cholesterol level was significantly higher for smokers than for nonsmokers ($P<.02$), and the ratio cholesterol/HDL-cholesterol was significantly higher for smokers ($P<.01$).

TABLE 10. RISK FACTORS IN SMOKERS AND NONSMOKERS*

Factor		N	Mean	S.D.	Percentile 2.5	Percentile 97.5
Cholesterol						
	A:	88	219.4	43.34	148	288
	B:	294	206.6	33.33	148	280
HDL						
	A:	88	231.6	58.74	148	356
	B:	292	246.1	65.63	146	403
Cholesterol/HDL-C						
	A:	88	5.0	1.50	2.72	8.73
	B:	292	4.5	1.30	2.42	7.66
Systolic BP						
	A:	88	121.3	14.24	94	160
	B:	294	122.2	12.72	100	148
Diastolic BP						
	A:	88	78.8	9.75	62	98
	B:	294	79.1	9.48	60	100
Ponderal Index						
	A:	88	12.53	0.45	11.43	13.45
	B:	294	12.55	0.42	11.73	13.28
Height						
	A:	88	70.7	2.22	69	75
	B:	294	70.6	2.08	69	75
Weight						
	A:	88	180.8	21.39	165	220
	B:	294	179.5	21.27	165	227

*A = smokers; B = nonsmokers

CONCLUSIONS

The purpose of the examination at this time was to establish in a select group of men firm baseline data relative to risk factors for coronary heart disease, and to do so at a time when the group was entering an age period of increasing risk of cardiac events. Clinical examinations performed on 382 members of the Cardiovascular Disease Followup Study resulted in objective findings of coronary artery disease in ten men. Five men had previously suffered a myocardial infarction, documented by medical records and electrocardiographic evidence. Coronary angiography showed that four men (of eight who underwent cardiac catheterization during the examination) had coronary disease--obstruction > 50% in one, < 50% in three. The tenth man had previously undergone coronary bypass surgery elsewhere after an evaluation by coronary angiography. The pattern of means of serum lipid and lipoprotein levels expected to be associated with coronary artery disease was found in this 10-man group; but because of the biological variability and the small number of men in the disease group, no definite conclusions were drawn about the meaning of these risk factors in this group.

The members of this study are not a cross section of U.S. males of comparable ages. This fact may be responsible for the disproportionately high prevalence of type A1 behavior pattern and the finding that in subjects classified as type A, the behavior pattern was not definitely correlated with elevation of any common risk factor for coronary artery disease. Further followup studies, coupled with the results of this examination and with previously collected serial data, should make an important contribution to understanding the relationship between an individual's history of changes in risk-factor levels and the development of cardiovascular disease in that individual.

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